Northwestern

Designs for Implementation Research Studies

Including Pilot, Small-n, and Developmental

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ISC3 Implementation Science Coordination, Consultation, & Collaboration Initiative

Center for Prevention Implementation Methodology
FOR DRUG ABUSE AND HIV

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NIMH: Implementation Research Institute (PI Proctor)

CDC: Raising Healthy Children Project (U18 DP006255, Smith & Berkel MPIs)

NHLBI: OpTIMISe–Child Hypertension (PI Smith)

Goals

- Basic understanding of various study designs for implementation research
  1) Pilot and developmental stage
  2) Larger trial designs
- Appreciation of key challenges in designing and conducting an implementation study

Publications

Designs and methods for implementation research: Advancing the mission of the CTSA program

Soohyun Hwang[1], Sarah A. Birken[1], Cathy L. Melvin[2], Catherine L. Rohweder[3] and Justin D. Smith[4]

An Overview of Research and Evaluation Designs for Dissemination and Implementation

Annual Review of Public Health
Vol. 38:1-22 (Volume publication date March 2017)
DOI: 10.1146/annurev-publhealth-031816-044215

C. Hendricks Brown,[1] Geoffrey Curran,[2] Lawrence A. Palinkas,[3] Gregory A. Aarons,[4] Kenneth B. Wells,[5] Loretta Jones,[6] Linda M. Collins,[7] Naihua Duan,[8] Brian S. Mittman,[9] Andrea Wallace,[10] Rachel G. Tabak,[11] Lori Ducharme,[12] David A. Chambers,[13] Gila Neta,[13] Tisha Wiley,[14] John Landsverk,[15] Ken Cheung,[16] and Gracelyn Cruden[1,17]

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Design and Analysis in Dissemination and Implementation Research

JOHN LANDSVERK, C. HENDRICKS BROWN, JUSTIN D. SMITH, PATRICIA CHAMBERLAIN, GEOFFREY M. CURRAN, LAWRENCE PALINKAS, MITSUNORI OGIHARA, SARA CZAJA, JEREMY D. GOLDHABER-FIEBERT, WOUTER VERMEER, LISA SALDANA, JENNIFER A. ROLLS REUTZ, AND SARAH MCCUE HORWITZ

AIDS and Behavior
https://doi.org/10.1007/s10461-019-02764-6

SUBSTANTIVE REVIEW

Landscape of HIV Implementation Research Funded by the National Institutes of Health: A Mapping Review of Project Abstracts

Justin D. Smith[1,2,7,8] · Dennis H. Li[2,3,8] · Lisa R. Hirschhorn[1,2] · Carlos Gallo[1,8] · Moira McNulty[4] · Gregory Phillips II[2,3] · Michelle Birkett[2,3] · Miriam Rafferty[1,5] · Amrita Rao[6] · Juan A. Villamar[1,8] · Stefan Baral[6] · Brian Mustanski[2,3,8] · C. Hendricks Brown[1,8] · Nanette D. Benbow[1,8]

Psychological Methods

1082-989X/12/$12.00 DOI: 10.1037/a0029312

Single-Case Experimental Designs: A Systematic Review of Published Research and Current Standards

Justin D. Smith
University of Oregon

Methodologies to Advance Health Equity

IMPLEMENTATION RESEARCH METHODOLOGIES FOR ACHIEVING SCIENTIFIC EQUITY AND HEALTH EQUITY

Moira McNulty, MD, MSc[1,2]; J.D. Smith, PhD[3,4]; Juan Villamar, MSEd[3,4]; Inger Burnett-Zeigler, PhD[3]; Wouter Vermeer, PhD[3,4]; Nanette Benbow, MAS[3,4]; Carlos Gallo, PhD[3,4]; Uri Wilensky, PhD[4,5]; Arthur Hjorth, PhD[4,5]; Brian Mustanski, PhD[3,4]; John Schneider, MD, MPH[1,2]; C. Hendricks Brown, PhD[3,4]

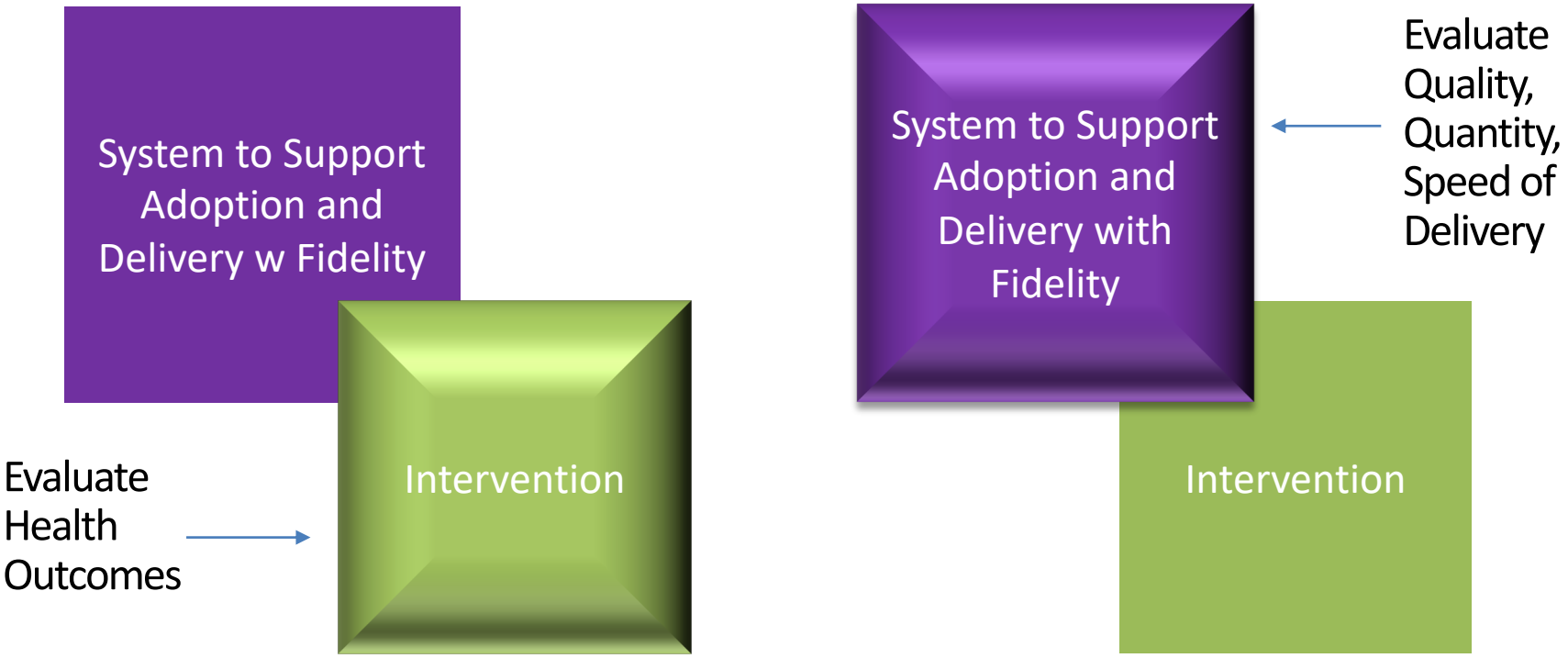
Brown, Smith, & Benbow

Covers the defining characteristics of trials testing implementation, provides a basic understanding of experimental designs for implementation research, and outlines the key challenges of designing and conducting an implementation trial.

http://cepim.northwestern.edu/trainings/

Implementation Research Has a Different Emphasis Than Other Types of Research

Effectiveness **vs.** **Implementation**



Influences what to measure, what to model, and what and how to test or evaluate

Terminology

- **Implementation research** evaluates of the use of strategies to integrate interventions into real-world settings to improve patient outcomes (generalizable knowl.)
- **Implementation preparation** studies are in preparation for a formal evaluation or test
  - Understand implementation processes, context, and barriers/facilitators
  - Explore the feasibility or acceptability of novel strategies
  - Development or tailoring of novel strategies
  - Adapting an EBI for context/population/delivery method
  - Modeling that has potential to inform IR

Brown et al. 2017; NIH, 2018; Smith et al. 2019

Design Terminology

- As used here, **design** refers to the planned set of procedures to
  - select subjects or larger units for study
  - assign these to or measure their naturally chosen conditions
  - assess measures before, during, and after assignment in the conduct of a study.

Hwang, Birken, Melvin, Rowheder, & **Smith**, 2020, *J Clin Trans Sci*

Community and Organizations Need to be Involved in Design Decisions and their Ownership

- Legal responsibility
- Moral responsibility
- Ethical responsibility

Key Areas

- developing and maintaining partnerships with diverse stakeholders
- recognizing under-resourced communities or other vulnerable populations have substantial historical trust concerns
- leadership is within a partnered participatory research framework
- methodological and design strategies that may apply when D&I research is conducted from a participatory, stakeholder perspective

Mensah, Cooper, Siega-Riz, Cooper, Smith, Brown et al. 2018

Designs for Implementation Research

- Examine how EBPs are adopted, scaled up, and sustained in community or service delivery systems

- Identify, develop, test, evaluate, and/or refine strategies to disseminate and implement evidence-based practices into public health, clinical practice, and community settings (NIH, 2019 in PAR-19-274, 275, 276)

  - Randomized and non-randomized designs
  - Hybrid effectiveness-implementation trials
  - Quality improvement designs for local knowledge
  - Simulation modeling

Brown et al. 2017; Landsverk, Brown, Smith, et al. 2017; NIH, 2019

Characteristics and Challenges of Implementation Research Trials

- External validity > internal validity
- Minimize disruptions to and burden on the systems
- Randomization occurs at "higher levels" of the service system (e.g., provider, clinic, county, etc.)
  - Small number of "units"
  - Nesting within multiple levels of the system(s)
  - Interactions between
- Experimental Designs: The implementation strategy/strategies are manipulated (serve as the IV)

Hwang, Birken, Melvin, Rowheder, & **Smith**, 2020, *J Clin Trans Sci*

Choosing a Design

- What design type is required to answer your implementation research question(s)?
  - Consider at what level in the system the primary outcome is measured (aligned with the level the strategy is targeting)
- Do you have sufficient units to answer your implementation research question(s)?
- Can you randomize the units?
- Is “implementation as usual” an acceptable comparison to your community/clinical partners?

When to Use

- Formative/Developmental

  Understanding context, selecting, tailoring, and adapting strategies for later testing
- Non-experimental

  Observational studies
- Within-site designs:

  generally simpler designs, typically not randomized
- Between-site designs:

  replication/aggregation, comparison of implementation strategies, randomization can reduce bias, produces generalized knowledge
- Within- and between-site designs:

  roll-out designs

  randomize timing (and potentially to implementation strategy)
- Hybrid effectiveness-implementation designs:

  many uses—when effectiveness data is still needed as implementation is studied or evaluated

Aims and Purposes of Small-n Implementation Research Studies

- Local knowledge
- Implementation preparation
  - Preliminary research on the feasibility and acceptability of novel strategies
  - Formative research to develop or tailor novel strategies
- Pilot testing the impact of a strategy
- Formative evaluation (Stetler et al., 2006)

Observational Studies, Formative Research, Simulation Modeling, Understanding Context

- Observational
  - Describes outcomes of interest and their antecedents in their natural context
  - Useful for evaluating the real-world applicability of evidence
- Formative Evaluation
  - A rigorous assessment process designed to identify potential and actual influences on the progress and effectiveness of implementation efforts (Stetler et al., 2006); commonly iterative and involve feedback to the system
  - Stakeholder-, expert-, and community-engaged activities (focus groups, stakeholder interviews, observation)
  - Useful for understanding context of implementation, selecting and tailoring implementation strategies
  - Example: Adapted ERIC Process (Go et al., 2016; Smith et al., 2020)
- Contextual Assessment (capacity, barriers/facilitators)
  - Describe and quantify characteristics of the implementation context
  - Used to understand the barriers, facilitators, and capacity of the context to align with the EBP, strategies, and outcomes (a la IRLM; Smith, Li, & Rafferty, 2020)
  - Surveys (ILS, ICS, OCRBS) and qualitative analysis (CFIR Interview Guide)
  - Can use formative evaluation methods

Sampling is critical for achieving appropriate representation of the variation in adopting sites and the engagement of stakeholders at multiple levels (leadership, managers, staff)

Simualtion Modeling

- A method for simulating the behavior of complex systems by describing the entities of a system and the behavioral rules that guide their interactions
- Offer a solution for understanding the drivers of implementation and the potential effects of different implementation strategies (without testing them)
  - Participatory system dynamics modeling (Zimmerman et al., 2016)
  - Network-based mathematical modeling (Jenness et al, 2016)
  - Agent-based modeling (McKay et al., 2018)

Within-Site Designs

Evaluating Change in a Single Site

Design Types and Definitions

- Post Design
  - Only measure implementation outputs after a new EBP is adopted
  - Common in quality improvement
- Pre-Post Design
  - Compare implementation outputs before and after a new strategy is used to deliver an EBP
- Interrupted Time-Series
  - Single unit quasi experiments m
  - Multiple baseline design

Post Design Example

- Can using PrEP active referral model between LHD STD Clinic and the PrEP clinic lead to completed appointments with a PrEP provider?
  - Target population: Patients with negative HIV test in combination and selected risk factors/STD results
  - Strategy: Active referral where STD clinic provider receives consent from client to provide contact information to PrEP clinic who then contacts client to schedule appointment with a PrEP provider
  - Comparison: No such services at baseline

Mikati et al. 2015

Example: Timeline for Post Design to Evaluate Impact

	Implementation Strategy	**Impacts**
No PrEP service (no referrals)	STD clinic partners with PrEP provider	1. Referrals to PrEP provider (adoption) 2. Completion of appointment with PrEP provider

Pre-Post Design

- Pre-Post Design testing the impact of an implementation strategy to sustain PrEP usage in LHD STD clinics
  - Example 1: Can the 38% of LHDs using PrEP increase long-term PreP usage?
  - Example 2: Can we improve linkage by adding a PrEP coordinator at the STD clinic who is responsible for identifying, counseling, and referring to PrEP clinic?

Interrupted Time-Series Designs

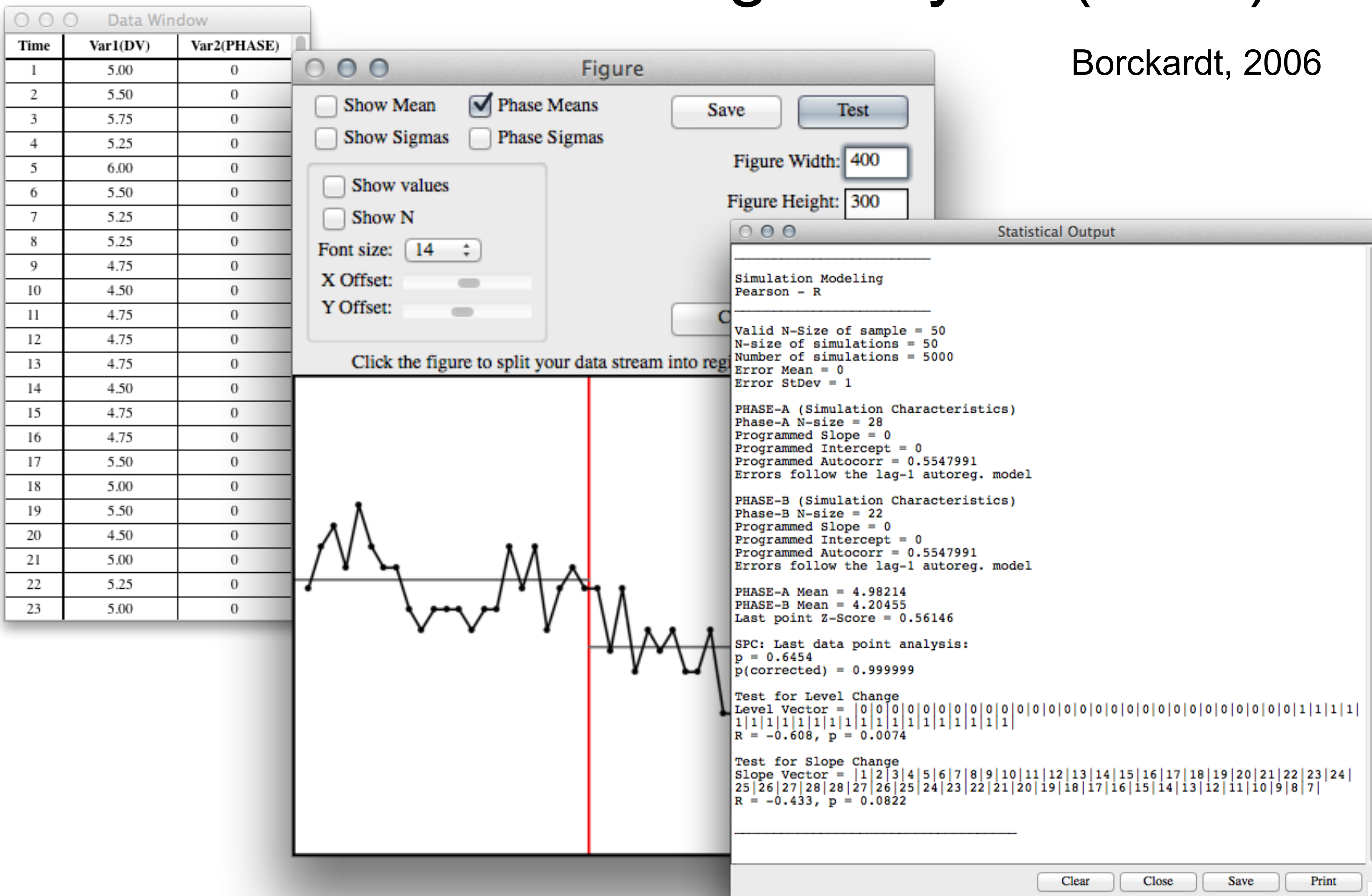
- "Single case" = a site/unit or a cluster of sites/units
- Primary Goal: determine whether a causal or functional relationship exists between the implementation strategy and outcomes

1. Does IV correspond to a change in level? (phase effect; level change)
2. Does IV correspond to a change in trajectory? (slope change)
3. Is change in one DV associated with another DV? (cross correlation)
   - Cases provide their own control data for the purpose of conducting a within-case comparison
     - Repeated, systematic assessment over time
     - Baseline or pre-implementation comparison
     - *Phases*

Smith, 2012

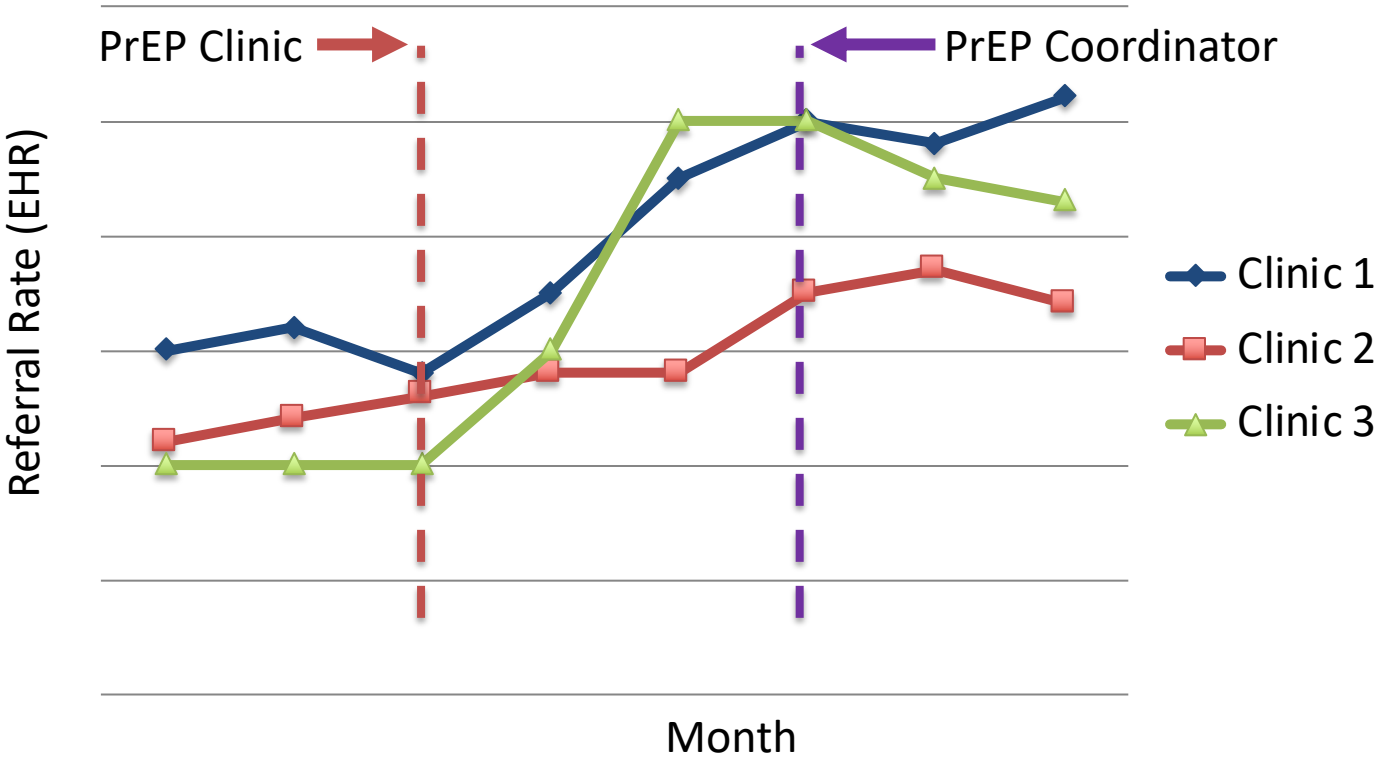
Simulation Modeling Analysis (SMA)

Borckardt, 2006



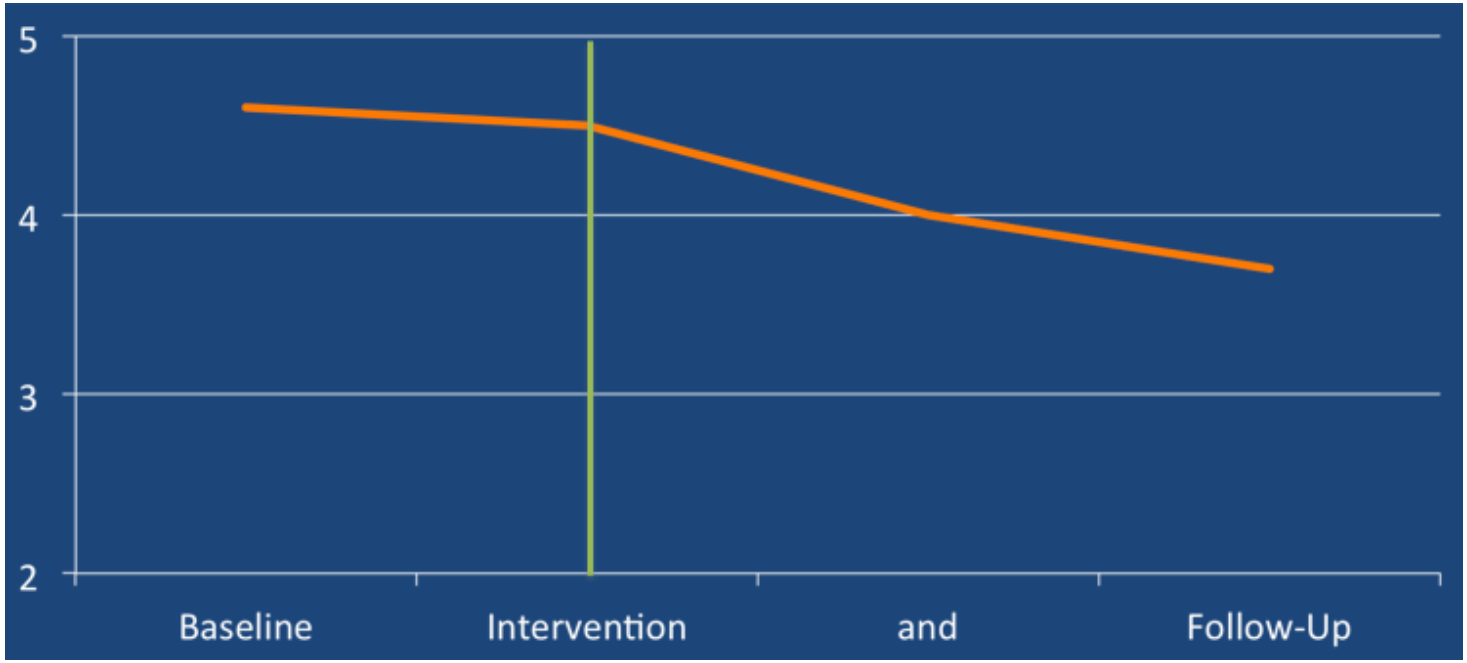
ITS Study Example

- Does adding a PrEP Coordinator to the clinic improve referral rates beyond partnering with a STI clinic for PrEP delivery?



Multilevel modeling (MLM)

(e.g., Shadish, Kyse, & Rindskopf, 2013)



- Non-concurrent, multiple baseline study involving 11 participants
- Significance of a change in trajectory and a change in level
- Estimate of the size of the effect

Smith et al. 2015

Summary of Within Site Designs

- Post, Pre-Post, Interrupted Time-Series Designs for novel interventions
  - Single site can demonstrate feasibility and initial impact
  - Multiple sites for full evaluation
- Rarely randomized (but possible)
- Simple and useful
- Local knowledge

Between-Site Designs

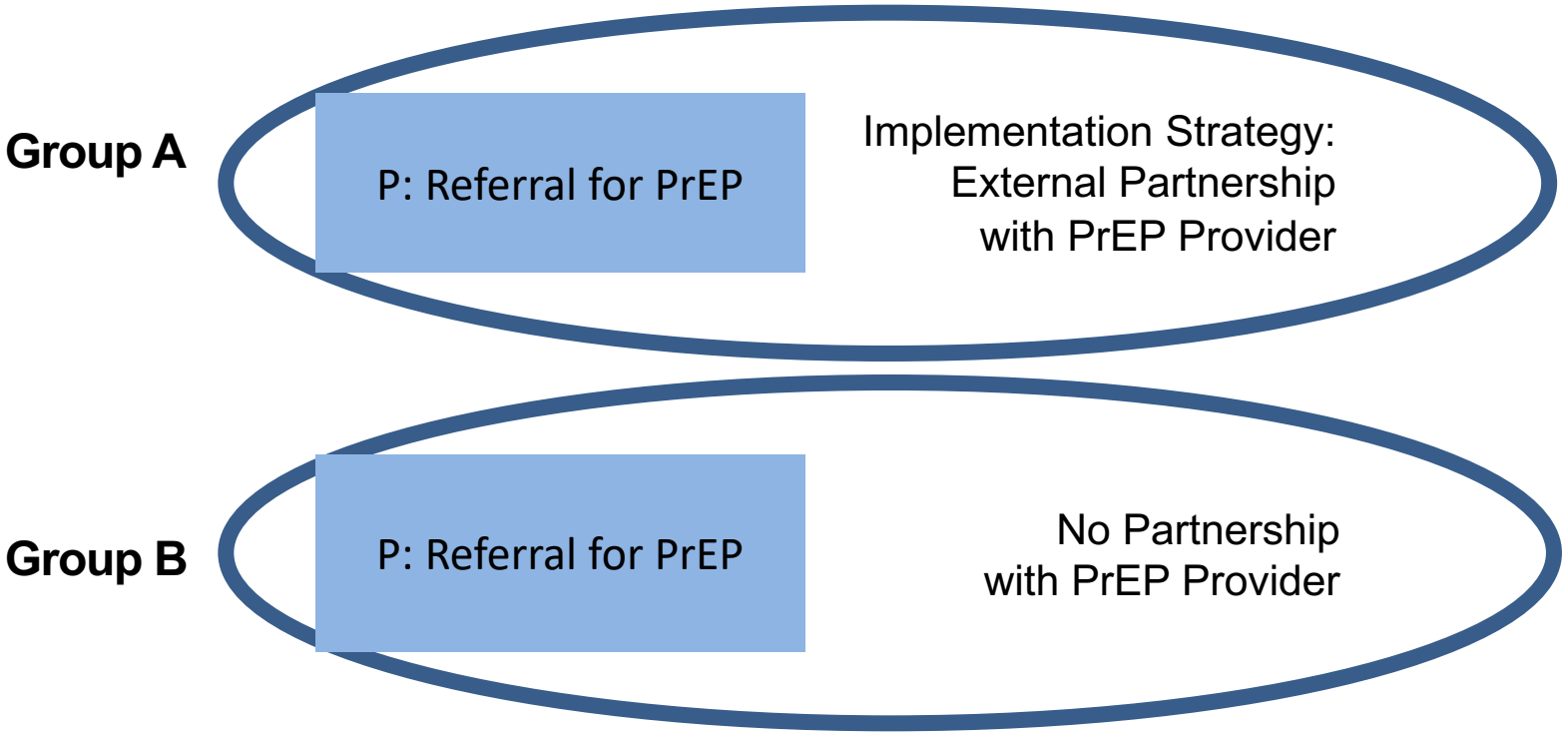
Compares Outcomes Between Two or More Sites

Design Types and Definitions

- Novel implementation strategy vs routine practice
  - Non-Randomized or Randomized
- Comparative Implementation
  - Two novel implementation strategies for the same clinical/preventive intervention (7 Ps)

- Common group-based study designs are applicable (e.g., cluster RCT), but with units at higher levels of the system (clinician, clinical team, clinic, hospital, county)

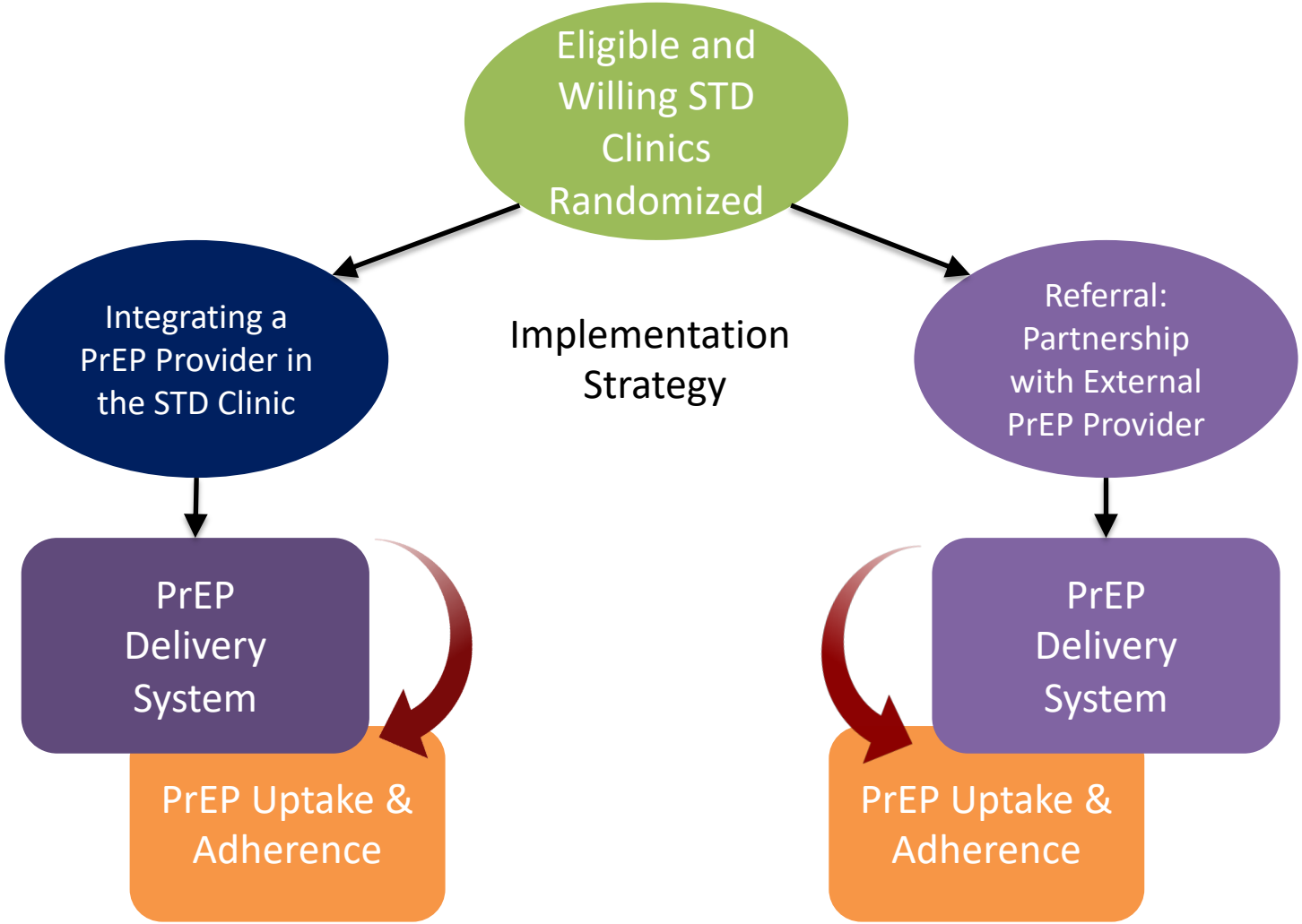
Novel Implementation Strategy vs Routine Practice using a Non-Randomized Implementation Design



Group A determined through self-selection/readiness, selective invitation, RFA

- High potential for introduction bias due to capacity/readiness

Design for a Randomized Comparative Implementation Trial

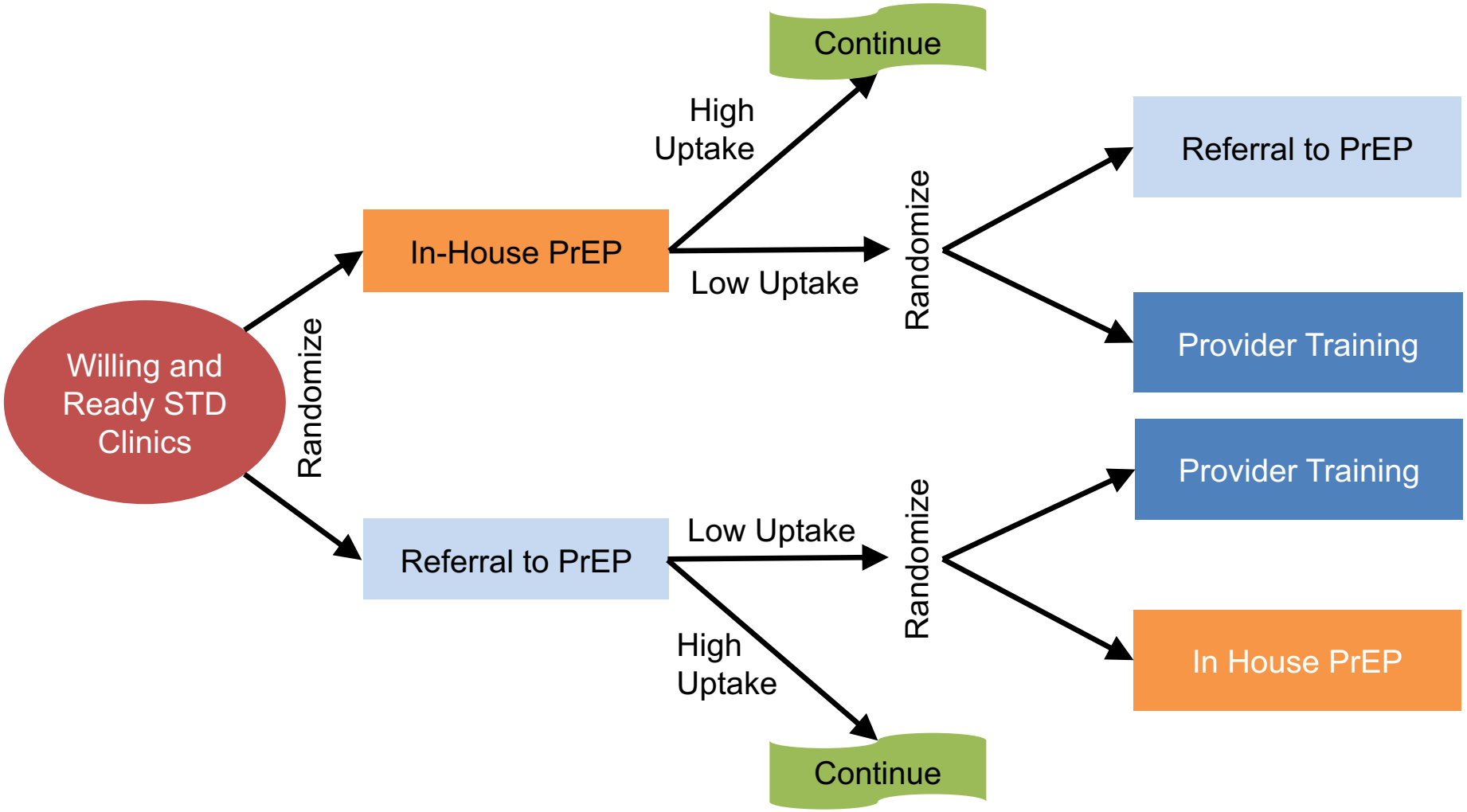


Testing and Optimizing Implementation Strategies: SMART Designs

- Sequential, multiple assignment, randomized trial (SMART)
- Optimization of dynamic and adaptive multicomponent implementation strategies
- SMART designs allow implementation strategies to be evaluated while responding to clinic's failure to reach impact

Collins, et al. 2014

SMART Design for PrEP Implementation in STD Clinics



Summary of Between Site Implementation Designs

- Used to compare the impacts of different implementation strategies across sites or groups of sites
- Contribute to generalizable knowledge

- Novel vs routine practice
  - Non-randomized
- Head-to-Head Comparison of Strategies
  - Equipoise
  - Randomization increases internal validity
- Incomplete Block Design
  - Use when few units are available
  - Randomization
- SMART Design
  - Adapt to address differential response to implementation strategies
  - Randomization

Within- and Between-Site Designs

(Roll-Out Designs)

Sites Begin as One Implementation Condition and Move to Another

Roll-Out Designs for Implementation Research

- Involves crossovers where units begin in one condition and move to another (within-site element), which is repeated across units (or clusters of units) with staggered crossover points (between-site element)
- Random, quasi-random, non-random assignment of all units in the study to the time when the implementation strategy will begin (i.e., the crossover)
- Units can be singular, clusters, matched pairs, others
- **Benefits of roll-out designs**
  - Reduce the logistic demands and resources needed in delivering new implementation strategies across multiple units
  - Equity (benefits for earlier and later start)
  - Beneficial to statistical power by using within and between comparisons of impacts
  - account for the effect of unanticipated confounders

Randomized Stepped Wedge Implementation Trial

Comparing Two Strategies (n=20 STD clinics)

	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
COHORT 1 (n = 4)	C	C	I	I	I	I	I	I	I	I	I	I
COHORT 2 (n = 4)	C	C	C	C	I	I	I	I	I	I	I	I
COHORT 3 (n = 4)	C	C	C	C	C	C	I	I	I	I	I	I
COHORT 4 (n = 4)	C	C	C	C	C	C	C	C	I	I	I	I
COHORT 5 (n = 4)	C	C	C	C	C	C	C	C	C	C	I	I

- Cohorts of 4 STD Clinics each (2 Refer to PrEP Provider, 2 provide in-house PrEP)
- Implementation staggered by 6 months for successive cohorts

Roll-Out Implementation Design (incomplete wedges)

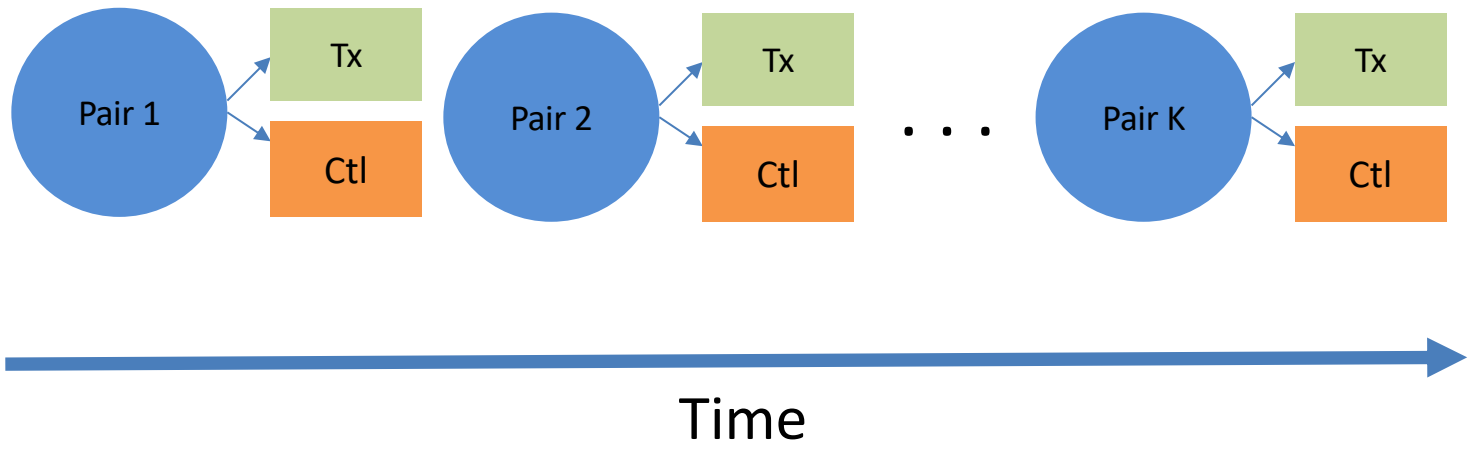
(n=28 Clinics, 7 clusters, 4 clinics each)

	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Cluster 1	C	C	I	I	I	I	I	I												
Cluster 2	C	C	C	C	I	I	I	I	I	I										
Cluster 3			C	C	C	C	I	I	I	I	I	I								
Cluster 4					C	C	C	C	I	I	I	I	I	I						
Cluster 5							C	C	C	C	I	I	I	I	I	I				
Cluster 6									C	C	C	C	I	I	I	I	I	I		
Cluster 7											C	C	I	I	I	I	I	I		

Incomplete wedge trials:

- Measurement begins immediately prior (e.g., 4–6 months) to the step rather than at T0
- Less burden on participating sites to collect data for long periods
- Allows researchers the option of staged enrollment in the trial if needed to achieve the full target sample (cumulative trials; Smith, Brown, et al., 2020)

Rollout of Repeated Pairs of Randomized Communities



Wyman et al. 2015; Brown et al. 2009